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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,914	08/10/2001	Timothy P. Tully	17VV-137270	5180

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	PAPER NUMBER
1627	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/927,914	TULLY ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-10,12,13,21,22,24-48,59,65-93 and 100-104* is/are pending in the application.

4a) Of the above claim(s) *2,9,10,12,13,21,22,24-48,59 and 65-93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-8 and 100-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/7/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/7/09 has been entered.

Claim(s) 3, 11, 14-20, 23, 49-58, 60-64, 94-99, 105-106 have been cancelled. Claim(s) 1-2, 4-10, 12-13, 21-22, 24-48, 59, 65-93, 100-104 are pending. Claim(s) 2, 9-10, 12-13, 21-22, 24-48, 59, 65-93 have been withdrawn. Claim 1 has been amended. Claim(s) 1, 4-8, 100-104 are examined herein.

Applicant's arguments have been fully considered but found not persuasive. The rejection(s) of the last Office Action are maintained for reasons of record and modified below as a result of the new claim amendments. The following new rejections will now apply.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification for the limitation "during rehabilitation of said animal from stroke and after the acute phase of said stroke in said animal has ended" as recited in Claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 1, 4-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent

protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation “administering to said animal before, during, and after said providing step”, and the claim also recites “wherein said administering occurs during rehabilitation of said animal from stroke and after the acute phase of said stroke" which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim(s) 100-104 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 100-104 depend on claim 98, which has been cancelled. Therefore, the metes and bounds of patent protection sought for this specific limitation has not been defined.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 4-8 are rejected under 35 U.S.C. 103(a) as being obvious over Christensen et al. (US Patent 5,547,979) in view of the Merck Manual (of record).

The instant claims are directed to a method of providing cognitive training and administering a phosphodiesterase 4 inhibitor to an animal during rehabilitation of said animal from stroke and after the acute phase of said stroke in said animal has ended.

Christensen et al. teach the phosphodiesterase inhibitor, rolipram (col. 11, line 14), in a method of treating stroke in a human (claim 1). The active ingredient may be administered from 1 to 6 times a day (col. 8, lines 62-64) or as recognized by one of ordinary skill in the art that the optimal quantity and spacing of individual dosages will be determined by the nature and extent of the condition, the form, route, site of

administration, patient, and that such optimums can be determined by conventional techniques (col. 10, lines 29-41).

It is noted that the limitations regarding "which enhances CREB pathway function" and "wherein rehabilitation of said cognitive deficit is effected by producing a long-lasting performance gain" are given little patentable weight, because these biological processes are inherent when the same compound is administered in the same patient population at the same dosage.

"Products of identical chemical composition can not have mutual exclusive properties." Any properties exhibited by or benefits from are not given any patentable weight over the prior art provided the composition is inherent. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the disclosed properties are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The burden is shifted to the applicant to show that the prior art product does not inherently possess the same properties as the instantly claimed product.

However, Christensen et al. fail to disclose multiple cognitive training sessions sufficient to produce an improvement in performance of a cognitive task whose deficit is associated with a central nervous system disorder to an animal during rehabilitation of said animal from stroke and after the acute phase of said stroke in said animal has ended.

The Merck Manual teaches that a training protocol should be started as early as possible towards a patient's rehabilitation to stroke. Such rehabilitation includes

encouragement, orientation toward the outside environment, eating, dressing, toilet functions, other basic needs, passive exercise, particularly of paralyzed limbs, and breathing exercises, if possible, should be started early (pg. 1455-1456). It is noted that these rehabilitation techniques meet the limitation of cognitive training. Furthermore, it is obvious to one of ordinary skill in the art to not stop at a single training session in the rehabilitation of a stroke victim since the process takes a great deal of time with many repeated sessions.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have combined the cognitive multiple training sessions, as described in the Merck Manual, before and during administration of the phosphodiesterase inhibitor, rolipram, in the method of treating stroke in a human, as disclosed by Christensen et al. during rehabilitation of said human from stroke and after the acute phase of said stroke in said human has ended.

A person of ordinary skill in the art would have been motivated to combine the cognitive multiple training sessions, as described in the Merck Manual, before and during administration of the phosphodiesterase inhibitor, rolipram, in the method of treating stroke in a human, as disclosed by Christensen et al. during rehabilitation of said human from stroke and after the acute phase of said stroke in said human has ended because: (1) both Christensen and the Merck Manual disclose treatment for the same purpose, which is treating stroke patients and because (2) of the additive therapeutic effects of employing two methods of treating stroke simultaneously. Therefore, one of ordinary skill in the art would have had a reasonable expectation of

success in treating stroke in a human by administering a phosphodiesterase inhibitor, rolipram, in conjunction with a cognitive training protocol, outlined by the Merck Manual during rehabilitation of said human from stroke and after the acute phase of said stroke in said human has ended.

Response to Arguments

Applicant argues that Christensen relates to administration of rolipram during the initial acute phase of a stroke episode to treat acute tissue injury. Christensen does not teach the administration of the compounds after the acute phase of the inflammatory event has ended or during training. Christensen along with the Merck Manual does not teach that one could achieve performance gain during the training by the administration of phosphodiesterase inhibitors before or during training. Specifically, Applicants go into great detail regarding the mechanism of action of PDE4 inhibitors, including inhibiting the inflammatory response often associated during the immediate time period following a brain injury. Therefore, Christensen effectively teaches away from the repeated application of PDE4 inhibitors in conjunction with stroke, due to the early production of TNF during the initial stages of an inflammatory event.

This is not persuasive for several reasons. At the outset, the amended claims still recite the administration of PDE4 inhibitors before, during, or after cognitive training, which means administration at any time during the treatment period. The claim then goes on to recite that the PDE4 inhibitor is administering during the rehabilitation phase of a stroke patient, which present several 112 issues as stated above. At any rate, the

cited prior art still reads on the instant claims because Christensen does not limit the administration of PDE4 inhibitors to any particular time period or treatment window of a stroke patient. In fact, Christensen clearly recites the treatment of a stroke patient, which also includes the time after the acute phase of stroke episode or the rehabilitation period involving cognitive training. Further, it is not clear when exactly does inflammation subside during the treatment period of a stroke patient, since low levels of inflammation could last well into the rehabilitation period. Applicant is reminded that the standard for obviousness is not absolute but a reasonable expectation of success.

Applicant argues that there is no reasonable expectation of success by combining the teachings of Christensen with cognitive training during rehabilitation. Applicant also argues that the Merck Manual can only be read to teach cognitive training after the acute phase of a stroke.

This is not persuasive because as stated above, Christensen clearly teaches, in general, the treatment of a stroke patient by administering a PDE4 inhibitor, which encompasses the entire treatment regimen including rehabilitation. Furthermore, the Merck Manual clearly state that a training protocol should be started as early as possible towards a patient's rehabilitation to stroke. Such rehabilitation includes encouragement, orientation toward the outside environment, eating, dressing, toilet functions, other basic needs, passive exercise, particularly of paralyzed limbs, and breathing exercises, if possible, should be started early. This time period may encompass when the patient is still in or just recovering from the acute phase of the stroke episode. Nonetheless, it is clear that the Merck Manual teaches cognitive

training after the acute phase of a stroke. It is Examiner's position that it would be obvious to administer PDE4 inhibitors as taught by Christensen in combination with rehabilitation after the acute phase of stroke. Therefore, since both references teach treating stoke patients, it is obvious to combine these treatment regimens because both are drawn to the same purpose as well as for the combined therapeutic effect. For these reasons, Examiner submits that there would be reasonable expectation of success in treating stroke patients as instantly claimed.

Applicant argues hindsight reconstruction in the argument that performance gain would necessarily result if rolipram therapy is administered immediately following stoke and cognitive therapy is begun as early as possible after stroke. Applicant argues that the Examiner has provided no evidence that the administration timeline contemplated by Christensen overlaps with that described by the Merck Manual. Specifically, Applicant argues that neither of the cited references teach or suggest "long-lasting performance gain effected by enhancement of CREB pathway function during rehabilitation."

This is not persuasive because said performance gain of a cognitive task in a stroke patient is an inherent property when the same compound is administered to the same patient at the same dose. Therefore, the "long lasting" and "enhancement of CREB pathway function" limitations are met because they are inherent properties. Moreover, the Examiner interprets performance gain of a cognitive task as covering a wide range of impairments, which include aphasia (language/speech disturbance) and apraxia (impaired ability to carry out motor activities), as disclosed in Applicant's own

disclosure. Essentially, the scope of the instant claims covers administration of the phosphodiesterase inhibitors at any time to the patient. Therefore, Applicant's assertion that Christensen is simply teaching the administration of rolipram during the acute phase of the stroke to reduce TNF still meets the limitations of the instant claims as it relates to the Merck Manual reference. Nonetheless, Applicant is invited to show factual data that performance gain would not result in the method taught by the cited prior art references.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Yong S. Chong/
Primary Examiner, Art Unit 1627

YSC